hybridizing the sample with a probe comprising at least 16 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide, and

detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

25. (Reiterated) A method of claim 24, wherein the probe comprises at least 30 contiguous nucleotides.

26. (Reiterated) A method of claim 24, wherein the probe comprises at least 60 contiguous nucleotides.

D3

27. (**Once Amended**) A [pharmaceutical] composition comprising a polypeptide of claim 1 in conjunction with a suitable pharmaceutical carrier.

REMARKS

Claims 1, 2, 14-18 and 21-27 are pending.

Claims 14-18 and 23-26 are withdrawn.

Claims 1, 2, 21, 22, and 27 are under active consideration.

Claim 1 has been amended to delete references to a naturally-occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1 or 2, and to a biologically-active or antigenically-active fragment of the amino acid sequence of SEQ ID NO:1 or 2. Claim 1 as amended recites a polypeptide comprising SEQ ID NO:1 or 2,and fragments of SEQ ID NO:1 or 2 comprising at least 15 amino acids, wherein said fragment binds specifically with an anti-PGAMP-1 or PGAMP-2 antibody. The "15 amino acids" language is supported in the specification at page 7, line 11.

Claim 2 has been amended so that in now recites a polypeptide having at least 90% amino acid sequence identity to SEQ ID NO:1 or 2 that binds specifically with an anti-PGAMP-1

antibody.

Applicant acknowledged finality of restriction and thanks examiner for her remarks regarding rejoinder of method claims.

At examiner's request, applicants submit copies of most of the references listed and lined-through in the IDS. Applicant does not have some of the Genbank references (numbers 22 and 23) at hand, and since these references are available on NCBI, which that examiner would have to access in any case if these references were to be considered again (in addition to analysis in the parent case), the applicant has not supplied them (but would be happy to do so if the examiner deems it necessary).

Claim Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 21, 22, and 27 were rejected because, allegedly, "the specification, while being enabling for the polypeptide having the amino acid sequences of SEQ ID NO:1 and SEQ ID NO:2, does not reasonable provide enablement for variants that have at least 90% sequence identity" with SEQ ID NO:1 and SEQ ID NO:2. And, allegedly, there is no guidance of how to make or use these variants. Examiner points out that such a claim will potentially encompass a vast collection of polypeptides and that the specification contains inadequate instructions to make and use these polypeptides without undue experimentation.

Claim 1 has been amended so that it no longer recites amino acid sequence having at least 90% sequence identity to a known sequence, making the rejection moot for Claim 1.

Claim 2 as amended now recites a polypeptide having at least 90% amino acid sequence identity to SEQ ID NO:1 that binds specifically with an anti-PGAMP-1 antibody. Applicants aver that the exact amino acid sequence of each and every sequence having 90% identity to SEQ ID NO:1 or 2 is known and can easily and routinely be listed using a simple computer algorithm. Although such a task may produce many pages of data, it is still routine, and would not be undue experimentation. SEQ ID NO:1 or 2 are two examples of such sequences. Applicant can supply a list of the other sequences should it be deemed necessary. Thus the specification does teach one of skill in the art how to make the claimed polypeptides.

The polypeptides claimed in the amended claims could be used, as described at page 49 et seq, to produce antibodies for detection of PGAMP-1, PAMG-2 and variants of such proteins in

a tissue sample, so as to identify hyperplasic prostate tissue (Northern analysis shows that 48% of the libraries in which PGAMP is expressed were made from hyperplasic prostate tissue, this is a highly significant correlation, much higher than one would expect by chance; see specification, page 14). Therefore the specification does teach one of skill in the art how to use the claimed polypeptides. In view of the present amendments and reasoning, applicants submit that the specification *does teach how to make and use* the claimed peptides, and applicants respectfully request that the rejection be withdrawn.

Claims 22 and 27 were rejected as not enabled for a "pharmaceutical" composition. The word "pharmaceutical" has been removed from the claims so that claims now simply claim a "composition." Applicants respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 21, 22, and 27 were rejected as allegedly indefinite because the terms "naturally-occurring" "biologically-active" and "antigenically-active" were deemed to be unclear. These terms have been removed from the amended claims, and instead the amended claims simply recite molecules that binds specifically with an anti-PGAMP-1 or anti-PAMGP-2 antibody. This language is not vague or indefinite and thus the rejection is overcome by the amendment and applicants respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 U.S.C. §102

Claim 1 was rejected under 102(b) as allegedly anticipated alternatively by Accession No. 20236, Yu et al, Andersson et al, or US Patent No. 5/723,315, which are all said to disclose a "fragment of the amino acid sequence of SEQ ID NO:1 or 2 "which would be antigenic and is the same as that claimed."

Applicants have no received any sequence comparison data (eg: MP SEARCH or BLAST data) and so are not certain exactly which fragments the examiner is claiming to anticipate the fragments of SEQ ID NO:1 and 2.

As amended, claim1 recites fragments of SEQ ID NO:1 and 2, comprising at least 15 amino acids, wherein said fragment binds specifically with an anti-PGAMP-1 or anti-PGAMP-2 antibody. It is believed that none of the cited references either teach or suggest such fragments,

and, since to anticipate a claim, each and every element of a claim must be taught, applicants respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 U.S.C. §103

Claim 27 was rejected as unpatentable over Accession No. 20236, Yu et al, Andersson et al, or US Patent No. 5/723,315, in view of Harlow and Lane. In view of the amendments (as explained in the paragraph above) applicants believe that the rejection is moot, and respectfully request that the rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650)855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Incyte Pharmaceuticals, Inc. Deposit Account No. **09-0108. This form is enclosed in duplicate.**

Respectfully submitted,

INCYTE PHARMACEUTICALS, INC.

Date: 22 May 2000

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